PCT/JP2003/011511

Translation

PATENT COOPERATION TREATY

PCT 10/527426

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3094WO0P	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/011511	International filing date (*day/month/year*) 09 September 2003 (09.09.2003)	Priority date (*day/month/year*) 10 September 2002 (10.09.2002)
International Patent Classification (IPC) or national classification and IPC C07D 263/32, 413/12, 413/14, 417/14, 417/12, 401/14, 403/12, C07F 7/18, 9/6558, A61K 31/422, 31/4439, 31/427, 31/4245, 31/454, 31/5377, 31/675, 31/695, 31/662, A61P 3/06, 3/04, 3/10, 9/12, 43/00		
Applicant TAKEDA CHEMICAL INDUSTRIES, LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 01 October 2003 (01.10.2003)	Date of completion of this report 21 April 2004 (21.04.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/011511

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 26, 28

because:

☒ the said international application, or the said claims Nos. 26, 28 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject matters of claims 26 and 28 relate to methods for treatment of the human body by therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 26, 28 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

The compounds that are encompassed in those described in claim 1 and at the same time useful for treatment of diabetes, etc., were well known prior to the filing of the present international application, as described in the cited documents in a separate sheet. The group of compounds, therefore, described in the Markush form in claim 1 do not have a new common chemical structure. Accordingly, claims 1, 16, 22, 25, 27 and 29 describe two or more different inventions, and it is not considered that they are so linked as to form a single general inventive concept.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☒ all parts.

☐ the parts relating to claims Nos. _____ .

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V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	11, 12, 15, 18-21, 29	YES
	Claims	1-10, 13, 14, 16, 17, 22-25, 27	NO
Inventive step (IS)	Claims	11, 12, 15	YES
	Claims	1-10, 13, 14, 16-25, 27, 29	NO
Industrial applicability (IA)	Claims	1-25, 27, 29	YES
	Claims		NO

2. Citations and explanations

Document 1: WO, 01-16111, A2 (Eli Lilly & Co.), 8 March, 2001 (08.03.01)
Document 2: WO, 01-00603, A1 (Glaxo Group, Ltd.), 4 January, 2001 (04.01.01)
Document 3: WO, 96-13264, A1 (Eli Lilly & Co.), 9 May, 1996 (09.05.96)
Document 4: US, 4171365, A (Sterling Drug, Inc.), 16 October, 1979 (16.10.79)
Document 5: GB, 2110211, A (F. Hoffmann-La Roche), 15 June, 1983 (15.06.83)
Document 6: Arzneim.-Forsch., 1978, Vol. 28, No. 5, pages 739-749
Document 7: Arzneim.-Forsch., 1978, Vol. 28, No. 3, pages 351-366
Document 8: JP, 63-159373, A (Nissan Chemical Industries, Ltd.), 2 July, 1998 (02.07.98)
Document 9: J. Med. Chem., 1986, Vol. 29, No. 6, pages 1065-1080
Document 10: US, 4996216, A (BASF AG), 26 February, 1991 (26.02.91)
Document 11: WO, 01-38325, A1 (Takeda Chemical Industries, Ltd.), 31 May, 2001 (31.05.01)
Document 12: US, 6214842, B2 (Michael S. Malamas), 10 April, 2001 (10.04.01)
Document 13: Chem. Pharm. Bull., 1 January, 2002 (01.01.02), Vol. 50, No. 1, pages 100-111
Document 14: J. Med. Chem., 28 March, 2002 (28.03.02), Vol. 45, No. 7, pages 1518-1534

Document 1 describes compounds useful as treatment drugs for hyperlipemia, non-insulin-dependent diabetes, diseases associated with insulin sensitivity, etc., and the compound of Example 2 corresponds to a compound represented by the formula (I) of the present application. Further, document 1 describes a pharmacological test result suggesting that the compound of Example 2 has an effect of lowering the blood sugar level.

Document 2 describes compounds useful as treatment drugs for hyperlipemia, diabetes, insulin resistance, obesity, etc., and the compound of Example 83 corresponds to a compound represented by the formula (I) of the present application.

Document 3 describes compounds useful as treatment drugs for hyperlipemia, diabetes, etc., and the compounds of Examples 6-8 and 8A correspond to compounds represented by the formula (I) of the present application. Further, document 3 describes a pharmacological test result suggesting that the compounds of Examples 6-8 have an effect of lowering the blood glucose level.

Document 4 describes compounds useful as anti-virus drugs, and the compound of Example 33 corresponds to a compound represented by the formula (I) of the present application.

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
W0 03/015774 A1 [E, X]	27.02.2003	15.08.2002	17.08.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 1 encompasses a large number of compounds. Only a small part of the claimed compounds, however, is supported by the specification according to PCT Article 6, and disclosed thereby according to PCT Article 5.

This International Preliminary Examination Report, therefore, only covers the part supported and disclosed by the specification, in other words, the compounds of the formula in claim 1 wherein R^1 is oxazole, thiazole, pyrazole or imidazole, X is a bond, Q is C_{1-6} alkylene, Y is oxygen atom, and Z is $-(CH_2)_n-Z^1-$ or $-Z^1-(CH_2)_n-$ (where Z^1 is not a bond).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : V.2

Document 5 describes compounds useful for treating Trypanosomatidae diseases and the compound of Example 6 corresponds to a compound represented by the formula (I) of the present application. Further, document 5 describes a pharmacological test result suggesting that the compound of Example 6 shows an activity of killing Trypanosomatidae.

Compound Nos. 183 and 185 described in document 6 correspond to compounds represented by the formula (I) of the present application. Document 6 also describes that compound No. 183 has an effect of curing infectious diseases of protozoans.

Compound No. 344 described in document 7 corresponds to a compound represented by the formula (I) of the present application. Document 7 also describes that compound No. 344 shows an anti-protozoan activity.

Compounds 283 and 284 in document 8 correspond to compounds represented by the formula (I) of the present application.

The compounds described in document 9, page 1078, right column, lines 59-61, correspond to compounds represented by the formula (I) of the present application.

Tables 1-3 and 6 of document 10 contain compounds that are encompassed in the formula (I) of the present application.

In view of the foregoing, the subject matters of claims 1-10, 13 and 14 do not appear to be novel in view of any of documents 1-10; the subject matter of claim 16 does not appear to be novel in view of any of document 1 or 3.

In view of the descriptions of documents 1-3, a person skilled in the art could have easily confirmed that the above-mentioned compounds have an effect of treating hyperlipemia, obesity, etc., and so the subject matters of claims 18-21 and 29 do not appear to involve an inventive step in view of documents 1-3.

None of documents 1-14 describes or suggests the compounds described in claims 11, 12 and 15 of the present application, and the said compounds would have been obvious a person skilled in the art.